REMARKS

Applicant has reviewed the Office Action dated March 19, 2010 and the comments of the United States Patent and Trademark Office ("Office") have been considered. In response, Applicant offers the following remarks.

Status of the Claims

Claims 15, 16 and 19-23 are currently pending and under consideration. Claim 1 is currently amended with support found in the Specification at page 4, for example. No new matter is introduced by this amendment.

Rejection under 35 U.S.C. § 112 – Written Description

Claims 15, 16 and 19-23 are rejected for allegedly lacking written description for negative provision "wherein said lipidic phase is not a product of reverse-phase evaporation." The Office alleges that this is not supported by the specification and is new matter. Applicant respectfully traverses.

Contrary to the Office's assertions, the methods of forming the liposomes of the present invention are detailed in the Specification at page 4, lines 6-10 and page 7, line 29 through page 8, line 7, for example. This is direct support for techniques that do not utilize the techniques of reverse-phase evaporation ("REV"). Moreover, the Specification discusses the undesired affects of using REV regarding a high loss of unencapsulated EPO (Specification at page 3, lines 2-12, specifically lines 10-12). Thus, the negative limitation of claim 15 is supported by a detailed method that does not include REV and the fact that the Specification does not teach using REV with the claimed products. For these reasons, the rejection is in error and should be withdrawn.

Rejection under 35 U.S.C. § 103(a)

The Office rejects claims 15, 16 and 19-23 for allegedly being unpatentable over:

I) JP 08 231417 ("'417") or Maitani 1996 ("Maitani") in view of JP 61097229 ("'229"); and

II) '417 in view of U.S. Patent 5,874,075 ("Collins") and further in view of '229.

Applicant respectfully traverses each rejection.

I. Rejection over '417 or Maitani in view of '229

This combination of references fails to teach or suggest all the requirements of the presently amended claims. Neither '417, Maitani nor '229 teach a composition wherein the lipidic phase is not a product of reverse-phase evaporation. In fact, '417 and Maitani specifically teach reverse-phase evaporation techniques that drive encapsulation of the active ingredient. The '229 reference does not remedy this deficiency because '229 does not teach lipidic phases or liposome formations. Moreover, neither '417, Maitani nor '229 teach a composition with "said active ingredient being dispersed within the aqueous phase and not within a liposome of the lipidic phase." The teachings of the '417 and Maitani directly contradict this by driving encapsulation with the use of REV in forming their preferred compositions. The '229 reference does not remedy this deficiency because the '229 reference does not rely on liposomal-based compositions as instantly claimed.

The combination of '417, Maitani and '229 fail to teach a lipidic phase that is not a product of REV. Moreover, the combination of '417, Maitani and '229 do not teach or suggest an "active ingredient being dispersed within the aqueous phase and not within a liposome of the

lipidic phase" as instantly claimed. Therefore, one of ordinary skill in the art would not look to the combination of '417, Maitani and '229 for making the presently claimed invention. All three references suffer the same deficiencies and therefore do not render the claims obvious. Therefore, the combination of references fails to meet the burden of establishing a *prima facie* case of obviousness regarding the claimed invention.

Even though all '417 and Maitani fail to teach all elements of the claimed invention, the Office alleges that it would be obvious to one of ordinary skill in the art to not remove active ingredient if so desired. While Applicant believes this argument to be moot in light of the currently amended claims and the arguments above, the fact remains that the main purpose of both '417 and Maitani is to drive encapsulation of the EPO by REV. The Office's assertion is mere conjecture in the absence of scientific rationale. The Office's opinion that one of ordinary skill in the art would not remove the free EPO if it was not necessary is not substantiated by evidence that meets the burden of obviousness. In fact, the '417 reference teaches that its invention provides "remarkable" results for the encapsulated EPO composition over the non-encapsulated EPO through their preferred methods (JP '417 after Table 1). Therefore, it appears that the Office's cited art provides incentive to one of ordinary skill in the art to remove the free EPO in practicing the '417 invention. This is a teaching away from the Office's assertion that one of ordinary skill in the art would be motivated to leave the free EPO. The Office has not proffered any scientifically-based rationale regarding the assertion that one of ordinary skill would simply leave the free EPO if it is not necessary to remove it.

As stated in the present Specification at page 3, lines 10-12, the use of REV to encapsulate EPO "suffers a high loss of unencapsulated EPO, which is undesirable and

expensive." Therefore, there would be no motivation for one of ordinary skill in the art to want to waste expensive free EPO in the practice of '417 and Maitani where REV is used to drive the encapsulation of EPO to form the preferred compositions of their teachings.

For at least the reasons discussed above, the Office has failed to meet the burden of establishing a *prima facie* case of obviousness, and Applicant respectfully requests that the rejection be withdrawn.

II. Rejection over '417 in view of Collins and further in view of '229

This combination of references fails to teach or suggest all the elements of the presently amended claims. In line with the discussion above, neither '417, Collins nor '229 teach, alone or in combination, a liposomal-based parenteral composition wherein the active ingredient (EPO) is "dispersed within the aqueous phase and not within a liposome of the lipidic phase" as presently claimed.

The '417 reference still fails to support a *prima facie* case of obvious for the reasons stated above. The '417 reference requires REV to drive EPO encapsulation and the '417 reference teaches this is how they acquire "remarkable" results. The '417 reference does not teach the active ingredient in the preferred composition as being dispersed within the aqueous phase and not within a liposome of the lipidic phase as presently claimed. The '417 reference specifically claims liposomes containing EPO. Under the Objective of the invention of '417, it is discussed that by encapsulating EPO with the REV method that the '417 invention attained the desired composition.

As stated above in Section I. there is no teaching in the '417 reference that would cause one of ordinary skill in the art to simple leave the free EPO in the solution. As discussed above and in the current Specification, EPO is expensive and waste is a drawback to the REV method regarding encapsulating EPO.

Collins does not remedy the shortcomings of the '417 reference because Collins fails to teach EPO being dispersed within the aqueous phase and not within a liposome of the lipidic phase as presently claimed. Collins does not specifically teach EPO as part of any specific liposomal-based parenteral composition. Moreover, Collins mentions EPO as part of a larger group of compounds that could be considered for use in the Collins invention. Collins does not provide any guidance regarding the use of EPO in the methods of Collins. Collins does not specifically claim or provide examples regarding EPO. Collins brief mentioning of EPO as a member of a larger group of compounds is nothing more than an invitation to experiment. There is simply a lack of information in Collins to offer one of ordinary skill the ability to practice Collins as to EPO. Collins requires very specific modifications for bonding/bridging select compounds to incorporate those select compounds into the membrane of the liposomes. This requires particular protein modifications discussed in Collins (Col. 8, ll. 8-25, for example); however, Collins does not offer any insight as how to perform these potential modifications to incorporate EPO into the membrane of the specific liposomes or lipid complexes disclosed in Collins. The Office is requiring one of ordinary skill to pick and choose from a large genus of compounds, including EPO, to combine Collins with any other reference to achieve the presently claimed invention. Contrary to the Office's assertion, this does not meet the burden of establishing a *prima facie* case of obviousness.

As admitted by the Office and taught in Collins, G-CSF is incorporated into the membrane of the lipid structure and is not dispersed in the aqueous phase as presently claimed. The Office's assertion that membrane-bound G-CSF is equivalent to the claimed EPO being dispersed in the aqueous phase is unsubstantiated and goes against the teachings of Collins and the present application. Collins does not teach dispersal of G-CSF in the aqueous phase but does teach incorporation of the G-CSF into the membrane. One of ordinary skill in the art would not look to Collins as teaching dispersal within the aqueous phase but would reasonably read Collins as requiring a level of chemical modification to specifically incorporate the G-CSF into the lipid membrane. One of ordinary skill in the art would read Collins as lacking any specific teachings regarding EPO being dispersed in an aqueous phase. Moreover, one of ordinary skill in the art would view Collins as invitation to experiment regarding incorporating EPO into the membrane, and would immediately realize that incorporation of EPO into the membrane is not equivalent to EPO being dispersed in the aqueous phase as presently claimed.

Despite the fact that Collins does not provide any specific guidance regarding most of the compounds mentioned in the large genus of contemplated compounds, the Office asserts that Collins teaches the compounds incubated with the liposomes "with an aqueous solution of the protein and if EPO attaches to the liposomal surface by some interaction, then EPO would behave the same way in instant invention also." Office Action Page 5. First and foremost, the Office offers no scientific rationale regarding this point. Second, Example 1 (Col. 14, ll. 1-17) definitively shows the steps taken to drive attachment and/or incorporation of G-CSF into the liposomal membrane. There is no mention of EPO and there is no evidence that this occurs merely by incubation of the liposome with the protein solution as proposed by the Office. This is

a baseless misinterpretation by the Office. Collins stresses that incubation under very specific conditions "is recommended (but not necessary)" based on the complexes being formed under the very specific steps and conditions that drive complex formation and/or membrane incorporation of the G-CSF in the steps immediately preceding the recommended incubation. *Id.* The Office's assertion that this incubation is equivalent to the presently claimed invention is an inappropriate misinterpretation of what is being taught by Collins regarding G-CSF.

The '229 reference does not teach a liposomal-based parenteral composition. The '229 reference does not teach an aqueous phase and buffer solution and a lipidic phase. Moreover, the '229 reference does not teach EPO dispersed in the aqueous phase and not within a liposome of the lipidic phase.

For the reasons stated *supra*, the references of '417, Collins and '229 fail to combine to form a *prima facie* case of obviousness regarding the claimed invention. For these reasons, Applicant respectfully requests the rejection be withdrawn.

CONCLUSION

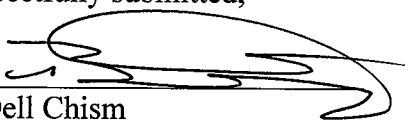
In view of the above amendment, Applicant believes the pending application is in condition for allowance.

Applicant submits concurrently a request for a two-month extension of time under 37 C.F.R. §1.136, and the accompanying fees. Please charge our Credit Card in the amount of $490.00 covering the fees set forth in and 1.17(a)(2). Should the Examiner have any questions or wish to discuss any issues, the Examiner is invited to contact the undersigned.

In the event that any additional extensions of time are necessary to prevent the abandonment of this patent application, then such extensions of time are petitioned. The U.S. Patent and Trademark Office is authorized to charge any additional fees that may be required in conjunction with this submission to Deposit Account No. 50-2228, under Order No. 026038.0240N1US from which the undersigned is authorized to draw.

Dated: August 19, 2010

Respectfully submitted,

By 

B. Dell Chism
Registration No.: 60,464
PATTON BOGGS LLP
8484 Westpark Drive, 9th Floor
McLean, Virginia 22102
(703) 744-8063
(703) 744-8001 (Fax)
Attorney for Applicant